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REMARKS

Claims 14-16, 20-23, 25, 27-31, 41, 42, 45 and 59-67 were pending in the above-identified application. By this Amendment, Applicants have amended claims 59, 66 and 67 and canceled claims 62-65 without prejudice or disclaimer to applicants' right to pursue these claims in the future. Accordingly, upon entry of this Amendment, claims 14-16, 20-23, 25, 27-31, 41, 42, 45, 60 and 61, and claims 59, 66 and 67, as amended, will be pending and under examination.

Support for new claim 59 may be found inter alia in the specification, as originally-filed, at page 58, line 33 through page 59, line 16; page 70, line 7 through page 78, line 10; page 82, line 29 through page 83, line 17; page 112, line 21 through page 114, line 8; page 167, line 31 through page 173, line 26; page 175, line 11 through page 177, line 5; page 189, line 14 through page 193, line 11; page 82, line 32 through page 183, line 4; page 188, line 60 through page 189, line 13; and page 207, line 28 through page 209, line 23. Support for new claim 66 may be found inter alia in the specification, as originally filed, at page 82, line 29 through page 83, line 17. Support for new claim 67 may be found inter alia in the specification, as originally filed, at page 112, line 21 through page 114, line 8.

Applicants therefore maintain that new claims 59, 66 and 67 raise no issue of new matter, are fully supported by the specification as originally filed, and request entry of these claims.

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Applicants note that the following grounds for rejection have been indicated to have been withdrawn in the September 16, 2003 Office Action:

1. the rejection under 35 U.S.C. § 112, first paragraph in paragraphs 9 and 10 of the last Office Action (par. 9 and 10);
2. the rejection under 35 U.S.C. § 112, second paragraph in paragraph 12 of the last Office Action (par. 12);

#### Previous Rejection

On page 2 of the Office Action, the Examiner acknowledged that there was a typo such that the rejection set forth in the last office was directed to R<sub>5</sub> but should have been directed to R<sub>7</sub>. The Examiner rejected claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59 and 60 under 35 U.S.C. § 112, first paragraph, alleging that the definition of R<sub>7</sub> where the aryl and heteroaryl of R<sub>7</sub> can be substituted with the moieties COR<sub>4</sub>, CO<sub>2</sub>R<sub>4</sub>, -CON(R<sub>4</sub>)<sub>2</sub>, -N(R<sub>4</sub>)<sub>2</sub>, -OR<sub>4</sub>, SR<sub>4</sub>, (CH<sub>2</sub>)<sub>o</sub>OR<sub>4</sub>, (CH<sub>2</sub>)<sub>o</sub>SR<sub>4</sub>, are not described in the specification for the genus. The Examiner required applicants to cancel the new matter in reply to this Office Action.

In response, in an attempt to advance the prosecution of the subject application, applicants have removed the following moieties from the definition of R<sub>7</sub>: -COR<sub>4</sub>; -SR<sub>4</sub>; -(CH<sub>2</sub>)<sub>o</sub>OR<sub>4</sub>; and -(CH<sub>2</sub>)<sub>o</sub>SR<sub>4</sub>, and amended the following moieties within the

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definition of  $R_7$ :  $-\text{CO}_2\text{R}_4$  with  $-\text{CO}_2\text{CH}_3$ ;  $-\text{CON}(\text{R}_4)_2$  with  $-\text{CONH}_2$ ;  $-\text{OR}_4$  with  $-\text{OCH}_3$ ;  $-\text{SR}_3$  with  $-\text{SCH}_3$ ; and  $-\text{N}(\text{R}_4)_2$  with  $\text{NH}_2$ . Furthermore, applicants have removed the following moieties from the definition of  $R_5$ :  $-\text{COR}_3$ ;  $-(\text{CH}_2)_o\text{OR}_3$ ; and  $-(\text{CH}_2)_o\text{SR}_3$ , and amended the following moieties within the definition of  $R_7$ :  $-\text{CO}_2\text{R}_3$  with  $-\text{CO}_2\text{CH}_3$ ;  $-\text{CON}(\text{R}_3)_2$  with  $-\text{CONH}_2$ ;  $-\text{OR}_3$  with  $-\text{OCH}_3$ ;  $-\text{SR}_3$  with  $-\text{SCH}_3$ ; and  $\text{N}(\text{R}_3)_2$  with  $-\text{NH}_2$ . Applicants maintain that new claim 59 is described in inter alia in the specification, as originally-filed, at page 58, line 33 through page 59, line 16; page 70, line 7 through page 78, line 10; page 82, line 29 through page 83, line 17; page 112, line 21 through page 114, line 8; page 167, line 31 through page 173, line 26; page 175, line 11 through page 177, line 5; page 189, line 14 through page 193, line 11; page 82, line 32 through page 183, line 4; page 188, line 60 through page 189, line 13; and page 207, line 28 through page 209, line 23. and respectfully request that this ground of rejection be reconsidered and withdrawn.

#### **Provisional Obviousness-Type Doubling Patenting Rejection**

On page 3 of the September 16, 2003 Office Action, the Examiner provisionally rejected claims 14-16, 20-23, 25, 27-31, 41, 42, 45 and 59-67 under the judicially created doctrine of obviousness-type double patenting as unpatentable over the claims of co-pending Application U.S. Serial No. 09/730,458. The Examiner acknowledged that the conflicting claims are not identical, but alleged that the claims are not patentably distinct from each other because the compounds, compositions and method of use of the instant invention are embraced by the

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compounds, compositions and method of use of copending application No. 09/730,458.

In response, applicants respectfully point out that where a "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that ground of rejection and permit the application to issue as a patent, thereby converting the 'provisional' double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." See Manual of Patent Examining Procedure § 822.01, under the heading "Only Provisional Double Patenting Rejection Remaining In One Application." Applicants further point out that copending Application U.S. Serial No. 09/730,458 is not currently in condition for allowance. Therefore, applicants respectfully request that the Examiner reconsider and withdraw this provisional ground of rejection and permit this application to issue.

#### Specification

On page 4 of the Office Action, the Examiner objected to the disclosure because of the page 251 had holes punched through the text.

In response, applicants have amended the specification to substitute original page 251 with replacement page 251, attached hereto as **Exhibit 1**. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this

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objection.

**Rejection under 35 U.S.C. 112**

On page 4 of the Office Action, the Examiner rejected claims 66 and 67 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleged that the addition of the species in claims 66 and 67 are not described in the specification for the genus.

In response, in attempt to advance the prosecution of the subject application, applicants have corrected the structures of previous claims 66 and 67 to match their descriptions on page 82, line 29 through page 83, line 17, and page 112, line 21 through page 114, line 8, respectively.

On page 5 of the Office Action, the Examiner rejected claims 14-16 20-23, 25, 27-31, 41, 42, 45 and 59-67 under 35 U.S.C. § 112, second paragraph, second paragraph, as being indefinite for allegedly failing to point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleged the following:

- a. Claims 14-16 20-23, 25, 27-31, 41, 42, 45 and 59-67 are vague and indefinite in that it is not known what is meant by the definition of  $R_1$  where  $R_1$  is  $-\text{CON}(R_4)_2$ . The Examiner believed that the applicants intended subscript 2.

- b. Claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59 and 60 are vague and indefinite in that it is not known what is meant by the definition of  $R_5$  where the aryl and heteroaryl of  $R_5$  can be substituted with F; Cl; Br; I;  $COR_3$ ;  $CO_2R_3$ ;  $-CON(R_3)_2$ ; CN; ...;  $N(R_3)_2$ ; ...;  $(CH_2)_oOR_3$ ;  $(CH_2)_oSR_3$  where there is no indication of the point of attachment for these moieties as shown by all of the other definitions within the claim.
- c. Claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59 and 60 are vague and indefinite in that it is not known what is meant by the variable "o" within the moieties of the substituents on  $R_5$ , i.e.  $(CH_2)_oOR_3$  and  $(CH_2)_oSR_3$ , which is not defined within the claim.
- d. Claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59 and 60 are vague and indefinite in that it is not known what is meant by the definition of  $R_7$  where the aryl and heteroaryl of  $R_5$  can be substituted with F; Cl; Br; I;  $COR_4$ ;  $CO_2R_4$ ;  $-CON(R_4)_2$ ; CN; ...;  $N(R_4)_2$ ; ...;  $(CH_2)_oOR_4$ ;  $(CH_2)_oSR_4$  where there is no indication of the point of attachment for these moieties as shown by all of the other definitions within the claim.
- e. Claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59 and 60 are vague and indefinite in that it is not known what is meant by the variable "o" within the moieties of the substituents on  $R_7$ , i.e.  $(CH_2)_oOR_3$  and  $(CH_2)_oSR_3$ , which is not defined within the claim.

In response to the Examiner's ground of rejection for point (a), in an attempt to advance prosecution, applicants have corrected

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the typographical error that the Examiner discovered. Applicants have amended the definition of  $R_1$  in amended claim 59 to recite " $-\text{CON}(R_4)_2$ ".

Furthermore, in response to the Examiner's ground of rejection for points (b) and (d), applicants have expressly designated the point of attachment for the substituents. Applicants have amended the definitions of  $R_5$  and  $R_7$  in amended claim 59 to expressly note the atom of attachment. Applicants maintain that support for amended claim 59 is described in the specification, as originally-filed, on page 58, line 33 through page 59, line 16

In response to the Examiner's ground of rejection for points (c) and (e), applicants note that amended claim 59 does not recite the variable "o", thereby rendering this objection moot.

Applicants maintain that amended claim 59 overcomes these grounds of rejection and respectfully request that these grounds of rejection be reconsidered and withdrawn.

#### Rejection under 35 U.S.C. §102

On page 6 of the Office Action, the Examiner rejected claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59, 60 and 62-65 under 35 U.S.C. 102(e) as being anticipated by Nagarathnam et al., U.S. Patent No. 5,942,517. The Examiner alleged that Nagarathnam teaches the compounds, compositions and method of use of the instant invention where B is (4-methoxyphenyl)methylthio as shown by examples 1-4.



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In response, in an attempt to advance the prosecution of the subject application, applicants have amended previous claim 1 to exclude (methoxyphenyl)methylthio (i.e.,  $-\text{SCH}_2\text{C}_6\text{H}_4\text{OR}_4$ ) as a choice for the definition of B and have further canceled claims 62-65. Applicants maintain that the pending claims are novel over Nagarathnam et al., U.S. Patent No. 5,942,517.

#### Rejection under 35 U.S.C. §103

On page 6 of the Office Action, the Examiner rejected claims 14-16 20-23, 25, 27-31, 41, 42, 45, and 59-67 under 35 U.S.C. 103 as being unpatentable by Nagarathnam et al., U.S. Patent No. 5,942,517. The Examiner alleged that the generic structure of Nagarathnam encompasses the instantly claimed compounds as claimed herein. The Examiner further alleged that Examples 1-4 anticipates the claims of the instant invention as described above and examples 11, 18, 19, 23, etc. differ only in the nature A, B, R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> substituents. Column 8 defines A as 6 different ring moieties; B is H, straight chained or branched C<sub>1</sub>-C<sub>7</sub> alkyl, ...; R<sub>1</sub> is H, straight chained or branched C<sub>1</sub>-C<sub>7</sub> alkyl, ...; R<sub>2</sub> is H, straight chained or branched C<sub>1</sub>-C<sub>7</sub> alkyl, ...; R<sub>3</sub> is 9 different ring moieties.

The Examiner alleged that the compounds of the instant invention are generically embraced by Nagarathnam in view of the interchangeability of the A, B, R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> substituent of the pyrimidine ring system. The Examiner alleged that thus one of ordinary skill in the art at the time the invention was made would have been motivated to select for example methyl for the variable B as well as other possibilities from the generically

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disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

In response, applicants maintain that new claims 14-16 20-23, 25, 27-31, 41, 42, 45, 59, 60, 61, 66 and 67 are unobvious with respect to Nagarathnam et al., U.S. Patent No. 5,942,517. Although the compounds of the instant invention are generically embraced by Nagarathnam, they are inventive over this disclosure in light of the amended definition of  $R_3$ . Applicants further note that claims 62-65 have been canceled.

Applicants note that the Examiner alleged that U.S. Patent No. 5,942,517 teaches the interchangeability of the A, B,  $R_1$ ,  $R_2$  and  $R_3$  substituents of the pyrimidine ring system. The Examiner further alleged that selecting methyl for the variable B as well as other possibilities from the generically disclosed alternatives of the reference would afford compounds with equivalent potency.

In contrast to U.S. Patent No. 5,942,517, applicants note that  $R_3$  has been limited to one variable in the instant application, as opposed to 9 variables described for  $R_3$  in U.S. Patent No. 5,942,517. Applicants, therefore, maintain that it would not have been obvious to one skilled in the art to have been motivated to choose this one preferred  $R_3$  substituent over the 8 other described moieties to afford compounds with the most potent activity. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

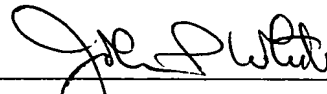
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In summary, in light of the remarks and amendments made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection and objection set forth in the September 16, 2003 Office Action and earnestly solicits allowance of the claims now pending in the subject application, namely claims 14-16, 20-23, 25, 27-31, 41, 42, 45, 60 and 61, and claims 59, 66 and 67, as amended.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

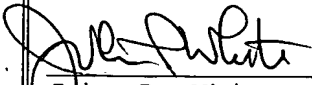
No fee is deemed necessary in connection with the filing of this Amendment. However, if a fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



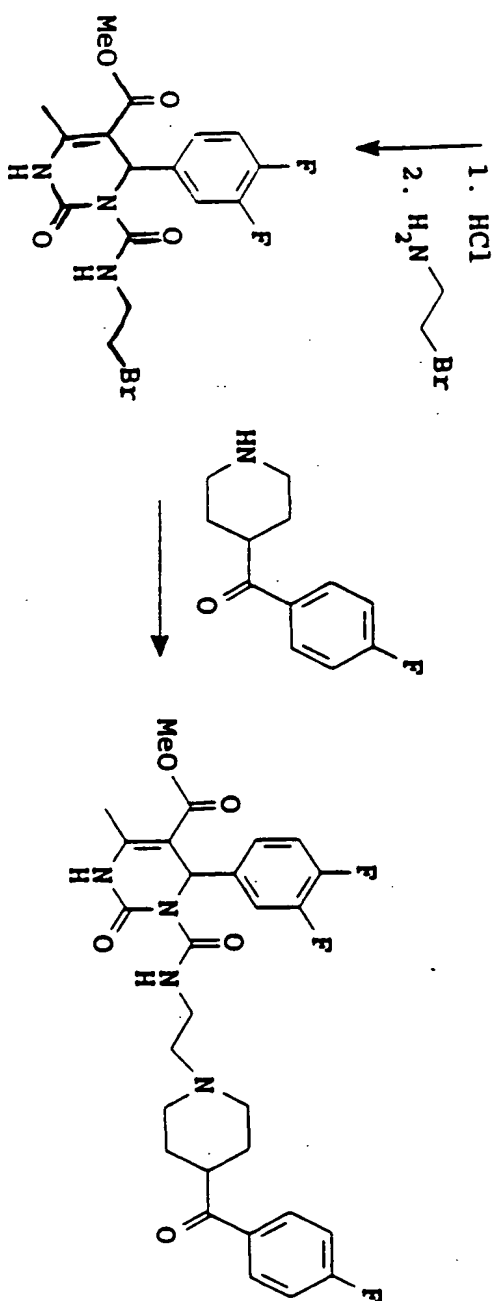
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**Scheme 12. General synthetic scheme for examples 30, 31, 35, 37, 39, 40, 47 and 48.**